



West, N., He, T., Hellin, N., Claydon, N., Seong, J., Macdonald, E., & Eusebio, R. (2018). Erosion Protection Efficacy of a 0.454% Stannous Fluoride Dentifrice versus an Arginine-Containing Dentifrice: Erosion Protection Efficacy of a SnF₂ Dentifrice . *American Journal of Dentistry*, 31(2), 63-66.

Peer reviewed version

[Link to publication record in Explore Bristol Research](#)
PDF-document

This is the author accepted manuscript (AAM). The final published version (version of record) is available online via AJD at <https://www.amjdent.com/Archive/Abstracts/2018/April%202018%20Abstracts.html#West> . Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research

General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
<http://www.bristol.ac.uk/pure/about/ebr-terms>

Erosion Protection Efficacy of a 0.454% Stannous Fluoride Dentifrice versus an Arginine-Containing Dentifrice

Nicola West, BDS, FDS RCS, PhD, FDS (Rest Dent)¹; Tao He, DDS, PhD²; Nikki Hellin, RDN¹; Nicholas Claydon, BDS, MScD, PhD¹; Joon Seong, BDS, MFDS RCPS¹; Emma Macdonald, HND, BSc, MSc, PhD¹; Rachelle Eusebio, MAS²

¹Clinical Trials Unit, Bristol Dental School, Lower Maudlin St, Bristol, UK.

²Procter & Gamble, Mason Business Center, Mason, OH USA.

Dr. West is Principal Investigator, Ms. Hellin and Dr. Macdonald are Dental Nurses, Dr. Seong is a Clinical Research Fellow and Dr. Claydon is a Clinical Teaching Fellow, University of Bristol Dental School and Hospital, Bristol, UK. Dr. He is a Principal Clinical Scientist and Ms. Eusebio is a Biostatistician, The Procter & Gamble Company, Mason, OH, USA.

Conflict of interest: Dr. He and Ms. Eusebio are full-time employees of the Procter & Gamble Company. Dr. West, Ms. Hellin, Dr. Claydon, Dr. Seong, and Dr. Emma Macdonald declare that they have no conflicts of interest.

Funding: The study was funded by the Procter & Gamble Company.

Short Title: Erosion Protection Efficacy of a SnF₂ Dentifrice

Key Words: in situ clinical, stannous fluoride, dental erosion, arginine

Corresponding Author:

NX West, BDS, FDS RCS, PhD, FDS (Rest Dent); Professor in Restorative Dentistry; Clinical Trials Unit; Bristol Dental School; Lower Maudlin Street, Bristol BS1 2LY UK

Email: N.X.West@bristol.ac.uk

Abstract

Objectives: To assess the anti-erosion effects of a 0.454% stannous fluoride dentifrice versus a marketed dentifrice in an *in situ* clinical study. **Methods:** This was a double-blind, randomized and controlled, two-treatment, four-period crossover clinical study involving healthy adults. Each study period was 10 days. Subjects were randomized to one of two dentifrice products each period: an experimental 0.454% stannous fluoride dentifrice (1100ppm fluoride) or a marketed 1.5% arginine-containing dentifrice (Colgate® Maximum Cavity Protection, 1450ppm fluoride). Subjects wore an intra-oral appliance fitted with 2 polished human enamel samples for 6 hours per day, swishing with the assigned dentifrice slurry twice a day in addition to sipping and swishing with 250ml of orange juice for 10 minutes (in increments of 25ml each minute) four times each day. Contact profilometry was used to measure surface changes of tooth enamel over the course of the study. Two measurements for each sample were taken at baseline and day 10. **Results:** Thirty-five subjects were randomized to treatment and 31 completed the study (mean age = 40 years). At day 10, enamel loss means were 0.128 µm for the stannous fluoride dentifrice and 1.377 µm for the arginine-containing dentifrice, respectively (p<0.001). This represents 90.7% less enamel loss for the stannous fluoride dentifrice. Both products were well tolerated. **Clinical Significance:** The 0.454% stannous fluoride dentifrice demonstrated significantly greater protection to human enamel against erosive acid challenges relative to the marketed 1.5% arginine-containing dentifrice in this *in situ* clinical study.

Introduction

Dental erosion is a clinical outcome resulting from a tooth demineralization process that is not the result of bacterial acids.¹ While bacterial acids initiate a reversible, subsurface demineralization process that can lead to caries, dietary acids, such as those found in carbonated drinks, energy drinks, sports drinks, citrus fruits and many other foodstuffs can overwhelm the natural, pellicle-coated tooth surface and induce a surface softening of the tooth mineral.² In addition to excessive exposure to acid-containing food and drink, excessive acid exposure that occurs as a result of gastro-esophageal reflux disease and bulimia has also been implicated as a contributory factor that can result in surface softening, and ultimately enamel loss of the teeth.^{3,4} Once lost, this mineral cannot be restored naturally; only with significant intervention from a dental professional can these irreversibly damaged surfaces be repaired.

While first noted on a wide scale in the United Kingdom during a national health survey of children,⁵ it is now clear that dental erosion has a global presence and is commonly found in both children and adults. Although a wide range of prevalence figures have been reported in different surveys, an average prevalence of around 30% of a population is not uncommon.^{6,7} Dental researchers have identified using oral care products to help prevent dental erosion. Oral care products help to deliver a protective barrier onto exposed tooth surfaces that can serve as either a sacrificial layer or as a coating to repel erosive acid challenges.⁸

Dentifrices formulated with stannous fluoride (SnF_2) have been shown in both laboratory and *in situ* clinical studies to be highly effective against both the initiation and progression of dental erosion.^{8,9-14} In these studies, the SnF_2 dentifrices tested demonstrated significantly greater

erosion protection benefits versus a wide range of dentifrice formulations. This benefit was recognized in a recent consensus report by the European Federation of Conservative Dentistry, noting that products formulated with SnF₂ have been shown to be effective at slowing the progression of erosive tooth wear, while data for other sources of fluoride were sparse.¹⁵ One of the proposed mechanisms of action for SnF₂ is through the deposition of an acid resistant smear layer onto exposed tooth surfaces via the attachment of the stannous ion to free phosphate sites at the enamel surface.

A dentifrice formulated with a combination of sodium monofluorophosphate (SMFP), arginine and calcium was recently shown to be more effective in two intraoral erosion models than an SMFP dentifrice that did not contain arginine and calcium.^{16,17} In those studies, however, there were no comparisons made against any SnF₂ dentifrices. The aim of the current study was to evaluate the relative abilities of an experimental, stabilized, 0.454% SnF₂ dentifrice and a marketed arginine-based, SMFP dentifrice to protect erosively challenged enamel specimens against surface enamel loss in a 10 day *in situ* clinical study.

Methods and Materials

Overview of in situ study

This was a single center, double-blind, randomized, supervised-usage, 2-treatment, 4-period crossover study. Before study initiation, a UK NHS Research Ethics Committee approved the study protocol (ISRCTN registry: ISRCTN55245733 DOI 10.1186/ISRCTN55245733). Thirty-five (35) healthy subjects consented to participate and enrolled following assessment of study inclusion and exclusion criteria. During the initial screening, study participants were provided

with a non-treatment, marketed dentifrice containing 0.32% NaF (1450 ppm fluoride - Crest® Decay Protection dentifrice^a), and a manual toothbrush (Oral-B®35 manual toothbrush^a) for use at home, in place of their normal oral care products during treatment periods in the morning prior to their study visits and again in the evening, as well as on weekends and on days off.

Test Products

Treatment dentifrices included in this study were:

- Experimental Dentifrice^a - 0.454% SnF₂ smooth texture (1100 ppm fluoride)^a
- Colgate® Maximum Cavity Protection^b – 1.1% SFMP (1450 ppm fluoride), sourced from the United Kingdom

Preparation of enamel specimens

All enamel specimens used in this study were prepared from caries-free, human, third molars that were donated by adult patients to a licensed tissue bank (Bristol Dental School and Hospital Tooth Tissue Bank, REC Ref: 11/N1/0145) following extraction. After receipt by the tissue bank, donated teeth were sterilized and roots removed for further use.

To prepare the enamel samples for insertion into the intraoral appliance, the disinfected tooth crowns obtained from the tissue bank were first sectioned into 1mm slices with a microslice.^c

The enamel slices were trimmed to fit into the appliance, as needed, using a high-speed handpiece and diamond bur. Each specimen was placed, test surface down, in a 6mm x 8mm x 2mm (width, length, thickness) mold, and the mold was filled with epoxy resin. After curing for 24 hours, specimens were removed from the mold and hand polished by a trained laboratory technician to a smooth and shiny finish using a standardized series of silicon-carbide papers,

silica powders and polishing techniques. Two readings were taken on each enamel sample using contact profilometry in order to obtain a baseline value for each specimen. A detailed description of the collection, preparation, sample tracking and analytical techniques used to measure the study specimens has been previously described by West et al.¹¹ At the end of the study (Day 10), specimens were again measured using the calibrated contact surface profilometer and a difference measurement was calculated. Fresh enamel samples were inserted into the appliance for each of the 4 test periods.

The intraoral appliance

Each study participant was specially fitted with an upper palatal intraoral appliance containing two of the prepared enamel samples. The appliance with the fitted enamel samples was worn on each treatment day of the study and was held in place using wire clasps that gripped onto suitable posterior teeth (Figure 1). On each of the 10 days of treatment, participants brushed their teeth at home, in their usual manner, with the non-treatment dentifrice. Once they arrived at the clinical site, participants collected their individually prepared appliance and inserted it into their mouth. Study participants wore the appliances for approximately 6 hours per day on each of the 10 treatment days of the study. Intraoral appliances were disinfected at the start and end of each treatment day using Corsodyl[®] mouthrinse (0.2% w/v chlorhexidine gluconate^d).

In situ product treatment

At the beginning of the study, participants were randomly assigned to a treatment sequence that ordered their use of the two test dentifrices. Twice each day (early morning and prior to lunch), personnel in the dispensing room at the clinical site prepared a slurry of the assigned test

dentifrice for each individual participant by mixing 3 grams of dentifrice and 10mL of water. For each treatment, participants swished for 60 seconds, under the supervision of study personnel, with a freshly prepared dentifrice slurry (Figure 2). Participants removed the appliance over lunch, during which time they placed the appliance in a moist jar. No food or drink, with the exception of water, was consumed during any period while the appliance was in the mouth.

Participants were not aware of the identity of the dentifrices they were using during the study, and they were instructed not to discuss the physical characteristics of the dentifrices with other participants or study personnel. As an added measure of blinding, the investigator and study personnel performing and recording surface profilometry measurements were not permitted in the product dispensing room during treatments.

In situ erosive challenge

The erosive challenge occurred with the appliance in the mouth. Subjects were required to sip 25mL of orange juice^e over a timed minute, swish it around in their mouth to make sure it came into contact with the enamel specimens, and then spit it out. This was repeated 10 times during each erosive challenge so that a total of 250mL of orange juice was exposed to the enamel samples over each 10-minute period of erosive challenge. The erosive challenge took place a total of four times on each treatment day. (Figure 2)

Statistical efficacy analyses

The primary measure of efficacy in this study was dental erosion, measured by surface profilometry, at Day 10. For each subject, treatment period, and visit, the average of four erosion measurements was calculated using two replicate measurements from each of two enamel sections. Data were transformed using the natural log function to satisfy the normality assumption. A general linear mixed model was used to compare treatments with a statistical model that included period and treatment as fixed effects, baseline as covariate and subject as a random effect. From the statistical model, estimated means on the natural log scale were back-transformed by using the exponential function to obtain the estimated medians or 50th percentiles on the original scale (μm). Statistical comparisons were two-sided at a 5% significance level.

Results

Thirty-five subjects signed an informed consent form and were randomized to treatment. Thirty-one subjects completed the study. Three subjects voluntarily withdrew from the study and one subject dropped out during the first study period due to a probably-related, moderate-severity adverse event (lip swelling). Subjects ranged in age from 21 to 59 with an average of 40.3 years ($\text{SD}=13.5$). Twenty-six (74%) of the subjects were female.

At Day 10, the experimental SnF_2 dentifrice demonstrated a statistically significant ($p<0.001$) lower enamel loss with the estimated median dental erosion of $0.1280\ \mu\text{m}$ with 95% CI = (0.0935, 0.1751) for the experimental SnF_2 dentifrice and $1.3772\ \mu\text{m}$ with 95% CI = (1.0124, 1.8733) for the SMFP/arginine dentifrice. The experimental SnF_2 dentifrice provided 90.7% greater protection (based on dental enamel loss) relative to the marketed SMFP/arginine

dentifrice ($p < 0.001$). The analysis of dental erosion on the natural log scale and the estimated medians are summarized in Table 1. Figure 3 shows Distribution Box plots of enamel loss by treatment. Figure 4 shows Distribution Box Plots of natural log enamel loss by treatment.

Discussion

This study clearly confirmed the ability of the experimental, stabilized 0.454% SnF₂ dentifrice to protect the enamel surface from dietary acid erosion. Further, the study confirmed that this effect was greater than the marketed arginine-based product over the 10-day test period. Oral care products are used daily by most individuals and this type of usage pattern is perfectly suited to delivery product therapies that can deposit onto and be retained on exposed tooth surfaces for extended periods of time and help protect teeth against erosive acid challenges. Many modern fluoride-containing products have been shown to provide some level of erosion benefit.¹⁸ However, most of these studies have not compared the effectiveness of the tested formulations against those containing stannous actives. In studies that have included stannous actives, stabilized SnF₂ has been shown to provide a level of protection significantly greater than other sources of fluoride.^{9-14,19-21}

When delivered into the oral cavity, SnF₂ reacts with exposed tooth surfaces to deposit a protective barrier layer that is likely composed of either stannous oxide or stannous fluorophosphate, both of which are highly acid resistant.²² Products formulated with stabilized SnF₂ have been confirmed to deposit a long-lasting stannous-rich, acid resistant barrier layer on the enamel surface capable of withstanding erosive acid challenges for extended periods of time post treatment.^{9-14,19-21}

The marketed control dentifrice used in this study contains a combination of 1450ppm F as SMFP, 1.5% arginine and calcium carbonate and is promoted for its ability to provide enamel strengthening due, in part, to the product's claimed ability to neutralize plaque acids. Although two studies sponsored by the manufacturer have demonstrated some level of benefit against erosive acids for a formulation that contains SMFP and 8% arginine,^{16,17} neither of these studies included a comparison of the effectiveness of the SMFP-arginine formulation versus any dentifrices that contained a stabilized SnF₂ active. Well-controlled *in vitro* erosion prevention studies that included a stabilized SnF₂ comparator demonstrated highly significant differences, in favor of the SnF₂ dentifrice, when compared to similar products containing SMFP and up to 8% arginine^{19,20} A recent *in situ* erosion prevention clinical trial provided similar results, with the stabilized SnF₂ dentifrice included in that study performing significantly better than the SMFP/arginine comparator dentifrice.²¹

This study design used an *in situ* model that has been well-accepted and published to assess the erosion protection benefits from dentifrice chemistry.^{9,10,21,23} Both products in the study were used according to the same instructions, providing controlled test conditions to ascertain the single-variable chemical effects of the dentifrice against erosive acid challenge. Use of models designed to incorporate abrasion in addition to erosive conditions could be considered for future research.

Conclusion

In the present *in situ* clinical study, the experimental 0.454% SnF₂ dentifrice demonstrated significantly greater protection to human enamel against erosive acid challenges relative to the marketed 1.5% arginine-containing dentifrice.

- a.** The Procter & Gamble Company, Cincinnati, OH, USA
- b.** Colgate-Palmolive, New York, NY, USA
- c.** Ultra Tec Ltd, Santa Ana, California, USA
- d.** GlaxoSmithKline, Brentford, Middlesex, UK
- e.** Sainsbury's Supermarkets Ltd, London, UK

References

1. Ganss C. Definition of erosion and links to tooth wear. In: Lussi A. *Dental erosion*. Monogr Oral Sci, Basel: Karger, 2006; 9-16.
2. Lussi A, Carvalho TS. Erosive tooth wear – a Multifactorial condition of growing concern and increasing knowledge. In: Lussi A, Ganss C. *Erosive tooth wear*. Monogr Oral Sci, Basel: Karger, 2014; 1-15.
3. Moazzez R, Bartlett D, Anggiansah A. Dental erosion, gastro-oesophageal reflux disease and saliva: how are they related? *J Dent* 2004; 32: 489-494.
4. Bouquot JE, Seime RJ. Bulimia nervosa: dental perspectives. *Pract Periodontics Aesthet Dent* 1997; 9: 655-663.
5. Nunn JH, Gordon PH, Morris AJ, Pine CM, Walker A. Dental erosion - changing prevalence? A review of British National childrens' surveys. *Int J Paediatr Dent* 2003; 13: 98-105.
6. Bartlett DW, Lussi A, West NX, Bouchard P, Sanz M, Bourgeois D. Prevalence of tooth wear on buccal and lingual surfaces and possible risk factors in young European adults. *J Dent* 2013; 41: 1007-1013.
7. Salas MM, Nascimento GG, Huysmans MC, Demarco FF. Estimated prevalence of erosive tooth wear in permanent teeth of children and adolescents: an epidemiological systematic review and meta-regression analysis. *J Dent* 2015; 43:42-50.
8. Huysmans MCDNJM, Jager DHJ, Ruben JL, Unk DE, Klijn CP, Vieira AM. Reduction of erosive wear in situ by stannous fluoride-containing toothpaste. *Caries Res* 2011; 45: 518-523.
9. Hooper SM, Newcombe RG, Faller R, Eversole S, Addy M, West NX. The protective effects of toothpaste against erosion by orange juice: studies in situ and in vitro. *J Dent* 2007; 35: 476-481.
10. Bellamy PG, Harris R, Date RF, Mussett AJ, Manley A, Barker ML, Hellin N, West NX. In situ clinical evaluation of a stabilised, stannous fluoride dentifrice. *Int Dent J* 2014; 64(Suppl 1): 43-50.
11. West NX, Seong J, Hellin N, Eynon H, Barker ML, He T. A clinical study to measure anti-erosion properties of a stabilized stannous fluoride dentifrice relative to a sodium fluoride/triclosan dentifrice. *Int J Dent Hyg* 2017; 15: 113-119.
12. Khambe D, Eversole SL, Mills T, Faller RV. Protective effects of SnF₂ - Part II. Deposition and retention on pellicle-coated enamel. *Int Dent J* 2014; 64(Suppl 1): 11-15.

13. Faller RV, Eversole SL. Protective effects of SnF₂ - Part III. Mechanism of barrier layer attachment. *Int Dent J* 2014; 64(Suppl 1): 16-21.
14. Eversole SL, Saunders-Burkhardt K, Faller RV. Erosion prevention potential of an over-the-counter stabilized SnF₂ dentifrice compared to 5000ppm F prescription strength products. *J Clin Dent* 2015; 26: 44-49.
15. Carvalho TS, Colon P, Ganss C, Huysmans MC, Lussi A, Schlueter N, Schmalz G, Shellis PR, Björg Tveit A, Wiegand A. Consensus report of the European Federation of Conservative Dentistry: erosive tooth wear - diagnosis and management. *Clin Oral Investig* 2015; 19: 1557-1561.
16. Sullivan R, Rege A, Corby P, Klaczany G, Allen K, Hershkowitz D, Godder B, Wolff M. Evaluation of a dentifrice containing 8% arginine, calcium carbonate, and sodium monofluorophosphate to prevent enamel loss after erosive challenges using an intra-oral erosion model. *J Clin Dent* 2014; 25(1 Spec No A): A7-13.
17. Sullivan R, Rege A, Corby P, Klaczany G, Allen K, Hershkowitz D, Goldder B, Wolff M. Evaluation of a dentifrice containing 8% arginine, calcium carbonate, and sodium monofluorophosphate to repair acid-softened enamel using an intra-oral remineralization model. *J Clin Dent* 2014; 25(1 Spec No A): A14-19.
18. Huysmans MC, Young A, Ganss C. The role of fluoride in erosion therapy. In: Lussi A, Ganss C. *Erosive tooth wear*. Monogr Oral Sci. Basel: Karger, 2014; 230-243.
19. Faller RV, Eversole SL. Enamel protection from acid challenge – benefits of marketed fluoride dentifrices. *J Clin Dent* 2013; 24: 25-30.
20. Eversole SL, Saunders-Burkhardt K, Faller RV. Erosion protection comparison of stabilised SnF₂, mixed fluoride active and SMFP/arginine-containing dentifrices. *Int Dent J* 2014; 64 (Suppl 1): 22-28.
21. West NX, He T, Macdonald EL, Seong J, Hellin N, Barker ML, Eversole SL. Erosion protection benefits of stabilized SnF₂ dentifrice versus an arginine-sodium monofluorophosphate dentifrice: results from in vitro and in situ clinical studies. *Clin Oral Investig* 2017; 21: 533-540.
22. Magalhães AC, Wiegand A, Rios D, Buzalaf MA, Lussi A. Fluoride in dental erosion. In: Buzalaf M. *Fluoride and the oral environment*. Basel: Karger, 2011; 158-170.
23. American Dental Association. Acceptance Program Requirements: Products to help prevent or reduce enamel erosion. April 2017.

34.

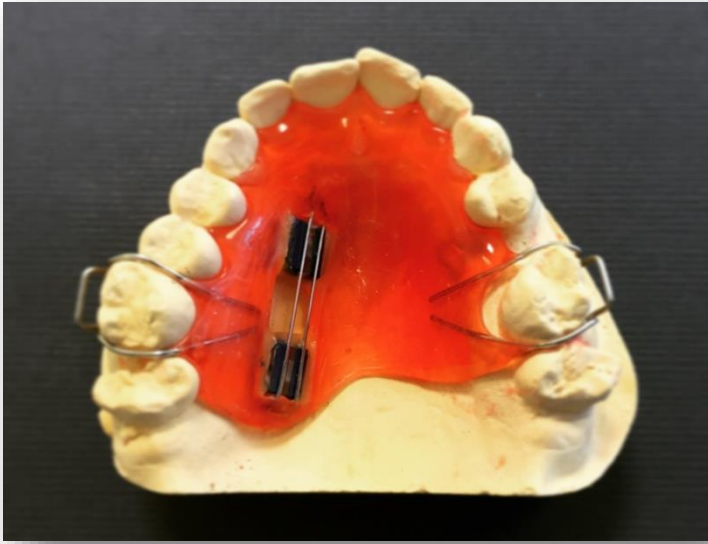


Figure 1. Intraoral appliance with two enamel specimens

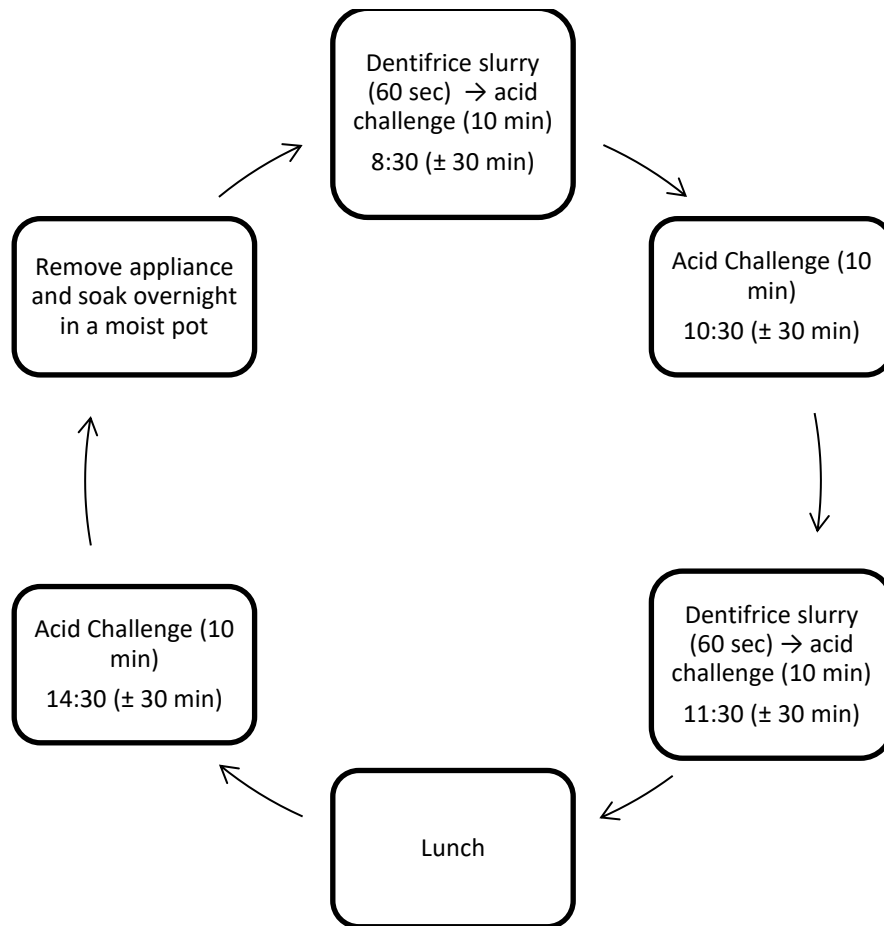


Figure 2. Daily treatment protocol

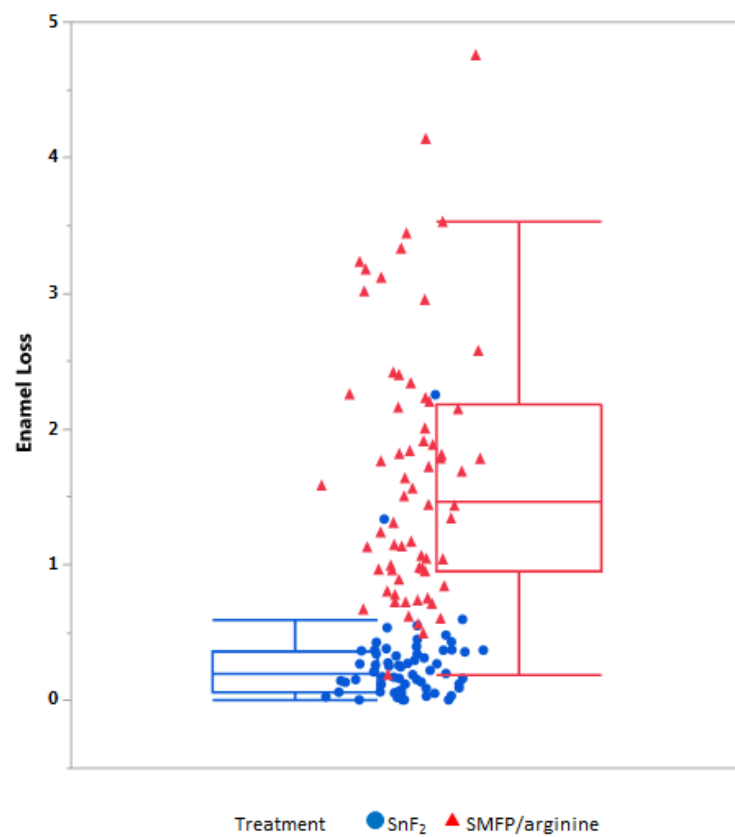


Figure 3. Distribution Box plots of enamel loss (µm) by treatment.

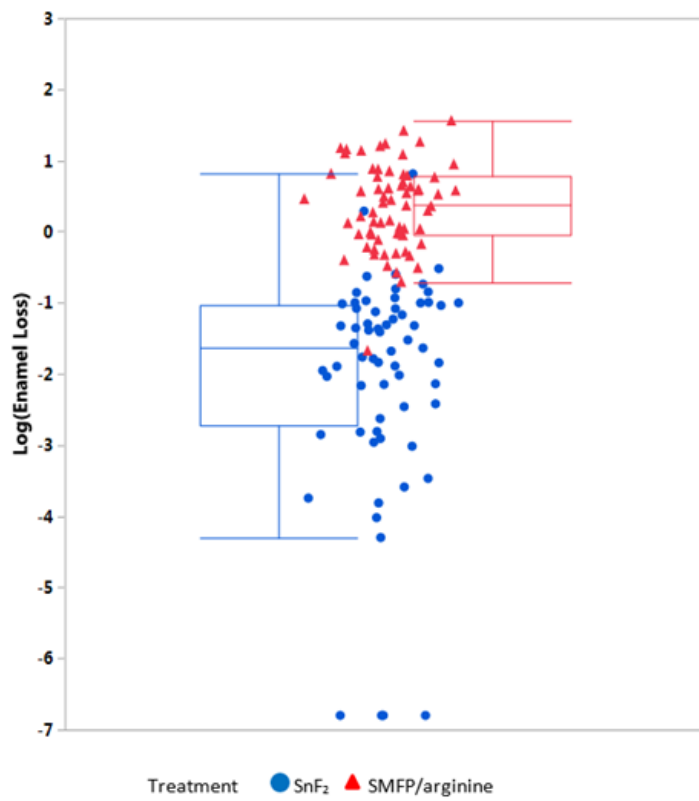


Figure 4. Distribution Box Plots of natural log enamel loss by treatment.

Table 1. Treatment Comparison of Profilometry Levels (μm)^a

Dentifrice Treatment	Original Scale in μm Estimated Median ^b	Natural Log Scale Mean (SE)	% Reduction vs. SMFP/ 1.5% arginine (<i>p</i> -value) ^c
10 Days Post-Baseline (Subject Variance = 0.3150, Residual Variance = 0.9764			
Experimental 0.454% SnF₂	0.1280	-2.0560 (0.1570)	90.7% (<i>p</i><0.001)
SMFP/ 1.5% arginine	1.3772	0.3200 (0.1539)	

^a Data were transformed using the natural log function to make the distribution bell-shaped before performing between-treatment analyses. Treatment and Period were fixed effects, Baseline was covariate and Subjects was a random effect. The carry-over effect was not statistically significant and was removed from the model.

^b Estimated medians in μm were obtained by using the exponential function on the means from the natural logarithmic scale.

^c Percent reduction was calculated using back-transformed means as 100% (SMFP-1.5% arginine – Experimental SnF₂ / SMFP-1.5% arginine). Two-sided *p*-values for testing the mean difference between treatments were provided.